COMMUNICATION

ChemComm
www.rsc.org/chemcomm

Unusually long cooperative chain of seven hydrogen bonds. An alternative packing type for symmetrical phenols

Praveen K. Thallapally,[a] Amy K. Katz,[b] H. L. Carrell[b] and Gautam R. Desiraju*[a]

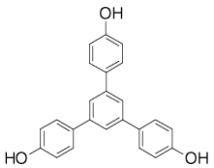
[a] *School of Chemistry, University of Hyderabad, Hyderabad 500 046, India. E-mail: desiraju@uohyd.ernet.in*

[b] *The Institute for Cancer Research, Fox Chase Cancer Center, 7701 Burholme Avenue, Philadelphia, PA 19111, USA*

Received (in Columbia, MO, USA) 5th November 2001, Accepted 12th December 2001
First published as an Advance Article on the web 24th January 2002

Conformational flexibility in a symmetrical tris-phenol leads to close packed structures that are also characterised by an extended though finite cooperative chain of hydrogen bonds.

When functional groups containing both hydrogen bond donors and acceptors (OH, CO_2H) are disposed symmetrically in a symmetrical molecular scaffold, open framework structures often result because this combination of molecular attributes is not compatible with Kitaigorodskii type bumps-in-hollows close packing.[1,2] The classical cases of β-quinol, phloroglucinol and trimesic acid,[3] and more recent examples[4–7] are representative. The close packing problem for these open frameworks is addressed by interpenetration and/or guest inclusion. Here, we report the crystal structures of 1,3,5-tris(4-hydroxyphenyl)benzene, **1**, and its 1:1 molecular complex, **2**, with 1,3,5-trinitrobenzene and discuss an alternative packing route for symmetrical phenols.



1

The crystal structure of tris-phenol, **1**, (Fig. 1)†‡ is *C*2/*c* (*Z*′ = 2) and all molecules lie on general positions. The structure is not of the open framework type. The most striking feature is a cooperative chain of five O–H···O hydrogen bonds (*b*, *c*, *d*, *e*, *f*). All six crystallographically distinct phenol residues are used in the formation of this chain. Fig. 2(top) shows that the O–H···O chain is preceded by a C–H···O hydrogen bond (***a***) and succeeded by a terminal O–H···π hydrogen bond (*g*) making a total of seven hydrogen bonds in a linear finite cooperative chain. This is unprecedented for a non-carbohydrate[8] and a survey of the CSD (Version 5.21, April 2001)[9] provides more details. The search was restricted to error free C–OH compounds with $R < 0.10$. Hydrates and disordered structures were included. Carboxylic acids and carbohydrates were excluded. Of the 4501 entries in this subset, infinite O–H···O motifs around 2_1 axes are overwhelmingly frequent. There are 68 hits with infinite motifs around 3_1 and pseudo-3_1 axes. The finite motifs include both cyclic and linear arrangements. In the former, closed trimers (11 hits, mean O–H···O 2.02 Å), tetramers (161 hits, 1.83 Å), hexamers (29 hits, 1.79 Å) and octamers (2 hits, 1.81 Å) are seen. Among the latter are found chains of three (36 hits) and four (15 hits) O–H···O hydrogen bonds. There are no cases of five or more O–H···O hydrogen bonds in a linear finite array. Further, in none of even the three and four O–H···O hydrogen bonded chains, do weaker bonds (C–H···O, O–H···π) form part of the cooperative system. To summarise, the present case is therefore quite unique.

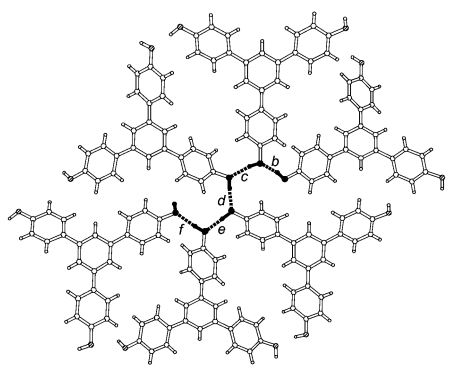


Fig. 1 Cooperative chain of five O–H···O hydrogen bonds in the crystal structure of tris-phenol **1**. The bonds are marked *b* through *f*. The six O–H groups involved are all crystallographically independent.

It is well known that in linear hydrogen bonded arrays, σ-cooperativity enhances the strengths of the individual hydrogen bonds.[10–12] This occurs through mutual polarisation of donors and acceptors along the chain such as $O^{\delta-}$–$H^{\delta+}$···$O^{\delta-}$–$H^{\delta+}$···$O^{\delta-}$–$H^{\delta+}$. With the inclusion of each additional hydrogen bond, the average strength of a bond in the array is further increased. This may be observed through computations (Table 1). With increasing hydrogen-bonded chain length, the non-bonded O···O distance decreases and the covalent O–H distance increases—effectively, the strength of the hydrogen bonds increase. However, there is an eventual fall off in the cooperative effect. The calculations show that the incremental effect decreases with each additional hydrogen bond and that there is a levelling out after five or six bonds. The structure of

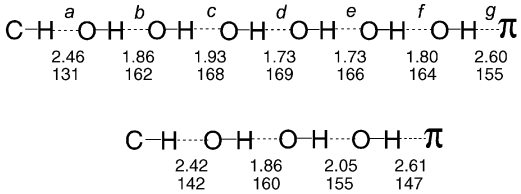


Fig. 2 Schematic view of the finite cooperative hydrogen bonded chains in this study. (Top) Seven hydrogen bonds (*a*–*g*) in structure **1**; (bottom) four hydrogen bonds in structure **2**. The bond metrics (Å, °) are indicated in each case.

Table 1 Calculations of mean hydrogen bond distances $D_{O\cdots O}$, covalent bond lengths r_{O-H} and hydrogen bond energies in linear cooperative arrays $(O–H\cdots)_n$ formed by methanol.[a]

n	$D_{O\cdots O}$ (Å)	r_{O-H} (Å)	Mean hydrogen bond energy/kcal mol^{-1}
1	—	0.946	—
2	2.944	0.950	5.53
3	2.903	0.952	5.81
4	2.894	0.953	6.65
5	2.887	0.953	6.73
6	2.877	0.954	6.90

[a] Calculations were performed in Spartan Pro[17] with a 6-31G* basis set.

DOI: 10.1039/b110036j

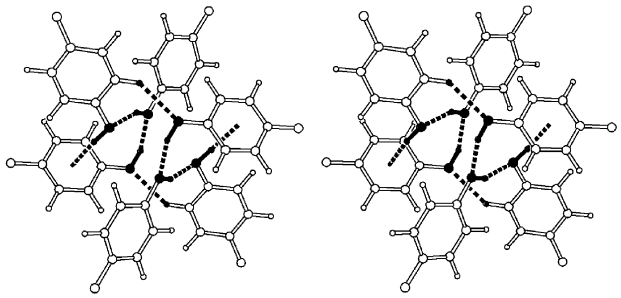


Fig. 3 Stereoview of the cooperative array of hydrogen bonds in structure **2**. Two centrosymmetrically related arrays are shown. Notice the commencing C–H···O bond and the terminal O–H···π bond as seen in structure **1**. The molecules are truncated for simplicity.

phenol **1** may therefore represent an optimal case wherein one obtains maximal stabilization from a finite array.

That the cooperative array in structure **1** is not an isolated example is seen from the crystal structure of the 1 : 1 complex **2**, formed by **1** and *sym*-trinitrobenzene. The structure is $P2_1/n$ (Z' = 1).‡ Fig. 3 is a stereoview that shows two cooperative chains of four hydrogen bonds each. The chain, shown in Fig. 2(bottom), commences with a C–H···O bond, continues with two O–H···O bonds and is terminated with a O–H···π bond to a phenyl ring. There are other C–H···O hydrogen bonds in this crystal structure, and this is common in molecular complexes of *sym*-trinitrobenzene,[13] but curiously this latter molecule is not involved in the cooperative network here. The metrics of the hydrogen bonds in structures **1** and **2** are comparable and in both cases, these bonds gain from the cooperative effect.

Why are these finite linear cooperative arrays formed? Unlike in other symmetrical molecules that form open frameworks,[5] the close packed structures observed for **1** and **2** could follow from the conformational properties of the O–H group. Usually, in simple phenols these properties lead to cyclic trimers, tetramers and hexamers or to their infinite chain variants.[14] Further conformational freedom of the aryl residues in **1** and **2** leads to extreme molecular flexibility. For example, the torsion angles of the O–H groups with respect to the phenyl rings are in the range 155–170° while the phenyl ring torsion angles are in the range 15–50°. All this conformational flexibility permits a wide variety of O–H···O, C–H···O and O–H···π hydrogen bonds accompanied by close packing of the aryl residues. The presence of the commencing and terminating C–H···O and O–H···π hydrogen bonds in both structures additionally suggests that the packing optimises all available strong and weak donors and acceptors.[11]§ The structures of **1** and **2** also appear to be quite stable. Calculations with the Polymorph Predictor program (Cerius^2)[15] give structures with three and four cooperative O–H···O hydrogen bonds if two molecules are included in the asymmetric unit. Indeed, the presence of symmetry independent molecules with the associated conformational variety may be what is needed to form these extended but finite hydrogen bonded chains.

Symmetrical molecules have long been used to construct open framework structures that may then interpenetrate and/or include guest molecules.[16] Here, and in contrast, we have described a symmetrical phenol which by virtue of its conformational flexibility is able to adopt a close-packed structure. The novel feature of this packing type is the presence of an unusually long finite cooperative chain of strong and weak hydrogen bonds. The stabilisation from co-operativity in these chains is equivalent to that provided by cyclic or infinite arrays of O–H···O hydrogen bonds in open framework structures while the close packing of hydrocarbon residues offers a stabilisation equivalent to that provided by interpenetration of the frameworks or by guest inclusion within the frameworks.¶ All in all, it may be reasonably expected that the structural features in **1** and **2** are likely to be observed in other similar conformationally flexible systems.

P K T thanks the CSIR for an SRF. AKK and HLC acknowledge financial support from grant CA-10925 of the NIH. G R D thanks Accelrys, Cambridge for continuing cooperation.

Notes and references

† Tris-phenol **1** was obtained by treatment of 4-hydroxyacetophenone with $SiCl_4$ in absolute EtOH at 0 °C for 6 h (S. Kotha, K. Chakraborty, E. Brahmachary, *Synlett*, 1999, 1621). We thank Professor S. Kotha (IIT Mumbai) for kindly providing a sample of this compound.

‡ *Crystal data* for **1**: 1,3,5-tris(*p*-hydroxytriphenyl)benzene ($C_{24}H_{18}O_3$, M = 354.38); monoclinic, space group $C2/c$, a = 28.922(2), b = 7.535(3), c = 33.815(7) Å, α = 90, β = 105.65(3), γ = 90°, V = 7096(3) Å^3, Z = 16, D_c = 1.327 Mg m^{-3}, T = 120 K, μ = 0.087 mm^{-1}, λ = (Mo-Kα) = 0.7107 Å, Nonius FAST area detector, 8885 unique reflections, 6596 with $F_o > 4\sigma(F_o)$, structure solution and refinement with SHELX97; H-atoms refined isotropically. Final R = 0.0521, wR = 0.1258.*Crystal data* for **2**: 1,3,5-tris(*p*-hydroxytriphenyl)benzene-1,3,5-trinitrobenzene 1 : 1 complex ($C_{30}H_{21}N_3O_9$, M = 567.50) monoclinic, space group $P2_1/n$, a = 14.534(3), b = 6.866(1), c = 24.375(5) Å, α = 90, β = 91.77(3), γ = 90°, V = 2431(8) Å^3, Z = 4, D_c = 1.550 Mg m^{-3}, T = 120 K, μ = 0.117 mm^{-1}, λ = (Mo-Kα) = 0.7107 Å, Nonius FAST area detector, 6040 unique reflections, 4837 with $F_o > 4\sigma(F_o)$, Structure solution and refinement with SHELX97; H-atoms refined isotropically. Final R = 0.0484, wR = 0.1210.CCDC 173734 and 173735. See http://www.rsc.org/suppdata/cc/b1/b110036j/ for crystallographic files in .cif or other electronic format.

§ Linear infinite O–H···O patterns are not seen here. Perhaps this is difficult in molecules with C_3 symmetry.

¶ The van der Waals, electrostatic and hydrogen bonded energies per molecule (Cerius^2, Minimizer, Dreiding 2.21 force field) in compound **1** and in phloroglucinol, respectively, are −26.88, −22.04, −8.75 kcal mol^{-1} and −10.57, −26.59, −9.42 kcal mol^{-1}.

1 G. R. Desiraju, in *Comprehensive Supramolecular Chemistry, Vol. 6 (Solid-state Supramolecular Chemistry: Crystal Engineering)*, ed. D. D. MacNicol, F. Toda and R. Bishop, Pergamon, Chichester, 1996, 1–22.

2 G. R. Desiraju, *Nature*, 2001, **412**, 397.

3 R. Bishop, *Chem. Soc. Rev.*, 1996, 311.

4 A. Nangia, *Curr. Opin. Solid State Mater. Sci.*, 2001, **5**, 115.

5 K. Kobayashi, T. Shirasaka, A. Sato, E. Horn and N. Furukawa, *Angew. Chem., Int. Ed.*, 1999, **38**, 3483.

6 M. R. Caira, A. Horne, L. R. Nassimbeni and F. Toda, *J. Chem. Soc., Perkin Trans. 2*, 1997, 1717.

7 E. Weber, M. Hecker, E. Koepp, W. Orlia, M. Czugler and I. Csöregh, *J. Chem. Soc., Perkin Trans. 2*, 1998, 1251.

8 H. S. Kim, G. A. Jeffrey and R. D. Rosenstein, *Acta Crystallogr., Sect. B, Struct. Sci.*, 1971, **27**, 307.

9 F. H. Allen and O. Kennard, *Chem. Des. Autom. News*, 1993, **8**, 1.

10 G. A. Jeffrey, *An Introduction to Hydrogen Bonding*, Oxford University Press, Oxford, 1997.

11 G. R. Desiraju and T. Steiner, *The Weak Hydrogen Bond in Structural Chemistry and Biology*, Oxford University Press, Oxford, 1999.

12 Many authors have referred to hydrogen bond cooperativity. The following recent papers contain many pertinent references: (*a*) P. Vishweshwar, A. Nangia and V. M. Lynch, *Chem. Commun.*, 2001, 179; (*b*) R. D. Parra, H. Zeng, J. Zhu, C. Zheng, X. C. Zeng and B. Gong, *Chem. Eur. J.*, 2001, **7**, 4352; (*c*) N. Kobko, L. Paraskevas, E. del Rio and J. J. Dannenberg, *J. Am. Chem. Soc.*, 2001, **123**, 4348; (*d*) S. Tsuzuki, H. Houjou, Y. Nagawa, M. Goto and K. Hiratani, *J. Am. Chem. Soc.*, 2001, **123**, 4255.

13 P. K. Thallapally, K. Chakraborty, H. L. Carrell, S. Kotha and G. R. Desiraju, *Tetrahedron*, 2000, **56**, 6721.

14 C. P. Brock and L. L. Duncan, *Chem. Mater.*, 1994, **6**, 1307.

15 Cerius^2, Accelrys, 9685 Scranton Road, San Diego, CA 92121-3752, USA. and 240/250 The Quorum, Barnwell Road, Cambridge CB5 8RE, UK.

16 For two interesting variations, however, see: (*a*) S. R. Batten, B. F. Hoskins, B. Moubaraki, K. S. Murray and R. Robson, *Chem. Commun.*, 2000, 1095; (*b*) R. Liu, K. F. Mok and S. Valiyaveettil, *New. J. Chem.*, 2001, **25**, 890.

17 Spartan Pro 1.0., Wave function Inc., 18401 von Karman Avenue, Suite 370, Irvine CA 92612, USA.